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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/561,043	12/12/2006	Antje Gupta	4838-002	3865

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EXAMINER	
MEAH, MOHAMMAD Y	

ART UNIT	PAPER NUMBER
1652	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/561,043	GUPTA ET AL.	
	Examiner	Art Unit	
	MD. YOUNUS MEAH	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 December 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-43* is/are pending in the application.

4a) Of the above claim(s) *13-40* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12 and 41-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/16/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

With preliminary amendment of this application, the applicant, on date 12/14/2007 elected without traverse Group I (claims 1-12) for examination and added new claims 41-43.

Election/Restriction

During preliminary amendment of this application, the applicant, on date 12/14/2007 elected without traverse Group I (claims 1-12), drawn to oxidoreductase comprising an amino acid sequence of SEQ ID NO: 9 for examination. New claims 41-43 fall in group I and will be examined herewith. Examiner acknowledge the typo error in election/restriction-office action of 11/14/07 that group I comprise oxidoreductase comprising "SEQ ID NO: 8", in fact it will be SEQ ID NO: 9 (SEQ ID NO: 8 is a DNA sequence). Groups II-VI (claims 13- 40) of election/restriction-office action of 11/14/07 is withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected Groups.

Priority

This application is a 371 of PCT /EP04/05831filled 05/28/2004, which claims priority on foreign applications Germany 103 27 454.5-41 filled 06/18/2003.

Information Disclosure Statement

The information disclosure statements (IDS) submitted on 12/16/2005, is in compliance with the provisions of 37 CFR 1.97. Accordingly, the examiner has considered the IDS statements.

Claim Rejections

35 U.S.C 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The claimed inventions in claims 1-12, 41-43 are rejected under 35 USC 101 because the claimed invention directed to non-statutory subject matter.

In the absence of the hand of man, naturally occurring protein, herein oxidoreductase, are non-statutory subject matter (Diamond v. Chakrabarty, 206 USPQ 193 (1980). The oxidoreductase of these claims is natural substance.

The rejection may be overcome by amending claims to recite wording such as an isolated oxidoreductase.

35 U.S.C 112 2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 41-43 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 41-43 are indefinite in the recitation of "stringent conditions" as the specification does not define what conditions constitute "stringent". While page 5 of the specification describes some conditions, which are intended to be stringent, there is nothing to suggest that other conditions would not also be included within the scope of this term and in the art what is considered stringent varies widely depending on the individual situation as well as the person making the determination. As such it is unclear how homologous to the sequence of a gene encoding SEQ ID NO: 9, a sequence must be to be included within the scope of these claims.

Claims 41-43, the phrase "complementary" renders the claims indefinite because it is unclear how much complementary a sequence is to that of SEQ ID NO: 8. fully or partially. It is suggested that applicants amend the claims to the phrase " fully complementary ".

35 U.S.C 112 1st Paragraph

Written Description

The following is a quotation of the first paragraph of 35 U.S.C. 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-2, 4-5 and 6-12, 41-43 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-2, 4-5 and 6-12, 41-43 are directed to a genus of oxidoreductase molecules (claims 1-2) or any oxidoreductase having one or more alteration of amino acid residues of SEQ ID NO: 9 or any oxidoreductase having 70% t0 80% sequence identity with SEQ ID NO:9 or any fragment thereof or any oxidoreductase coded by any DNA hybridizes under any stringent conditions with DNA comprising SEQ ID NO:8 or complementary strand thereof. The specification teaches the structure of only a few representative species of such oxidoreductase (i.e., SEQ ID NO: 9). Moreover, the specification fails to describe any other representative species by any identifying characteristics or properties other than the functionality of encoding a protein having reducing a carbonyl compound to (S) hydroxyl compound. Given this lack of description of representative species encompassed by the genus of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

In *University of California v. Eli Lilly & Co.*, 43 USPQ2d 1938, the Court of Appeals for the Federal Circuit has held that "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials". As indicated in MPEP § 2163, the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show that Applicant was in possession of the claimed genus. In addition, MPEP § 2163 states that a representative number of species means that the species, which are adequately described, are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.

Claims 1-2, 4-5 and 6-12, 41-43 comprise genus of oxidoreductase molecules (claims 1-2) or any oxidoreductase having one or more alteration addition to or subtraction of amino acid residues of SEQ ID NO: 9 or any oxidoreductase having 70% t0 80% sequence identity with SEQ ID NO:9 or any fragment thereof or any oxidoreductase coded by any DNA hybridizes under any stringent conditions with DNA comprising SEQ ID NO:8 or complementary strand thereof. The specification lacks description of all

these enormous variants of oxidoreductase species, especially oxidoreductase variants comprising many variations of SEQ ID NO:9 by mutation, addition , deletion or substitution of the amino acid residues of SEQ ID NO: 9 and identifying characteristics or properties or structure correlated with function. Therefore one of skill in the art would not recognize from the disclosure that applicants' were in possession of the claimed invention.

Applicants' are referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Enablement

Claim 1-2, 10-13, 41-43 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for oxidoreductase comprising SEQ ID NO: 9 or oxidoreductase having one or more alteration (addition or subtraction) of amino acid residues of SEQ ID NO: 9 or any oxidoreductase so that said oxidoreductase comprise an amino acid sequence having 90% sequence identity with SEQ ID NO:9 , does not reasonably provide enablement for any oxidoreductase molecules (having any structure, claims 1-2) or any oxidoreductase having any alteration of amino acid residues of SEQ ID NO: 9 or any oxidoreductase having 70% t0 80% sequence identity with SEQ ID NO:9 or any fragment thereof or any oxidoreductase coded by any DNA hybridizes under any stringent conditions with DNA

comprising SEQ ID NO:8 or complementary strand thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands* (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breath of the claim(s).

Claims 1-2, 10-13, 41-43 are so broad as to encompass any oxidoreductase molecules (having any structure, claims 1-2) or any oxidoreductase having many alteration of many amino acid residues of SEQ ID NO: 9 or any oxidoreductase having 70% t0 80% sequence identity with SEQ ID NO:9 or any fragment thereof or any oxidoreductase coded by any DNA hybridizes under any stringent conditions with DNA comprising SEQ ID NO:8 or complementary strand thereof. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number oxidoreductase broadly encompassed by the claims. In view of the great breaths of claims 1-2, 10-13, 41-43, amount of experimentation required to isolate polypeptide molecules having specific oxidoreductase activity from these enormous number of polypeptide molecules and , the lack of guidance, working examples, unpredictability of the art in predicting the function (oxidoreductase activity)

from protein's structure the claimed invention would require undue experimentation. As such the specification fails to teach one of ordinary skill how to use the full scope of the claims.

Since the amino acid sequence of a protein encoded by a polynucleotide determine its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the sequence and respective codons in its polynucleotide, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the encoded proteins' structure relates to its function. However, in this case the disclosure is limited to one oxidoreductase (SEQ ID NO: 9).

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompassed any oxidoreductase molecules (having any structure, claims 1-2) or

any oxidoreductase having any alteration of amino acid residues of SEQ ID NO: 9 or any oxidoreductase having 70% t0 80% sequence identity with SEQ ID NO:9 or any fragment thereof or any oxidoreductase coded by any DNA hybridizes under any stringent with DNA comprising SEQ ID NO:8 or complementary strand thereof because the specification does **not** establish: (A) regions of the polynucleotide/protein structure which may be modified without oxidoreductase activity; (B) the general tolerance of oxidoreductase to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any oxidoreductase residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any polypeptide molecules encoding any oxidoreductase having any structure, claims 1-2) or any oxidoreductase having any alteration of amino acid residues of SEQ ID NO: 9 or any oxidoreductase having 70% t0 80% sequence identity with SEQ ID NO:9 or any fragment thereof or any oxidoreductase coded by any DNA hybridizes under any stringent conditions with DNA comprising SEQ ID NO:8 or complementary strand thereof. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of a oxidoreductase gene, having the desired biological characteristics is unpredictable and

the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

CLAIM Rejection - 35 U.S.C 102

35 U.S.C 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1- 2 are rejected under 35 U.S.C. 102(b) as being anticipated by Xie et al. (*Biosci, Biotech. Biochem* 1999, 63, 1721-1729, from IDS). Xie et al. teach a NADH dependent oxidoreductase (Alcohol dehydrogenase, carbonyl reductase) isolated from *Nocardia fusca or Candida sp* (table 5) that reduce carbonyl compound to (S) - hydroxyl compound.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mohammad Meah whose telephone number is 571-272-1261. The examiner can normally be reached on 8:30-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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